40. (New) A prevention kit comprising an aqueous formulation of dextrin, wherein the prevention kit is useful for surgical use for the prevention of adhesions in animals or humans.

41. (New) A kit according to Claim 40, wherein the kit is biocompatible.

42. (New) A kit according to Claim 40, wherein the kit is bioresorbable.

43. (New) A kit according to Claim 40, wherein the kit is non-toxic.

Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action mailed May 21, 2002. Claims 1-39 are pending in the present application. Applicant has added new Claims 40-43. Support for new Claims 40-43 can be found in the claims and in the present application at page 7, lines 5-11, among other places. Applicant has cancelled Claim 36 for the purpose of rewriting. Applicant has also cancelled Claim 38. Applicant has also taken this opportunity to amend the specification to correct a typographical error on page 1, line 28.

Claims 26-34 and 38 stand rejected under 35 U.S.C. § 112, second paragraph. Claim 38 is objected to under 37 C.F.R. § 1.75(c). Claims 1, 2, 4-10, 12, 13, 17, 18, 22, and 36 stand rejected under 35 U.S.C. § 103. Claims 1, 3, 11, 14-16, 21, 22, 36, 37, and 39 stand rejected under 35 U.S.C. § 103. Claims 1, 19, and 20 stand rejected under 35 U.S.C. § 103. Claims 23-35 stand rejected under 35 U.S.C. § 103.

Applicant addresses each of these objections or rejections below.

I. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 26-34 and 38 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicant has amended Claim 23 to include a recitation that refers to "a composition," thus, providing antecedent basis for "said composition" and "the composition" recited in Claims 26-34. Amended Claim 23 also sets forth steps involved in the method of using the composition recited in the claims. Applicant has cancelled Claim 38. Applicant respectfully submits that these claim amendments are supported by the application as filed and respectfully request entry thereof.

Accordingly, Applicant respectfully requests that the rejection of Claims Claims 26-34 under 35 U.S.C. § 112, second paragraph, be withdrawn.

II. Claim Objections

Claim 38 is objected to under 37 C.F.R. § 1.75(c). As stated above, Applicant has cancelled Claim 38, and amended Claim 23 now recites steps involved in the method of using the composition as recited in the present claims. Therefore, Applicant respectfully requests that this objection be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

A. Claims 1, 2, 4-10, 12, 13, 17, 18, 22, and 36 are patentable under 35 U.S.C. § 103

Claims 1, 2, 4-10, 12, 13, 17, 18, 22, and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,258,175 to Davies (Davies). More specifically, at page 3, the Action states that "it would have been obvious to one of ordinary skill in this art at the time the invention was made having the Davies patent before him to obtain the claimed composition in view of the closely related structure of the dextrin derivative and similar components present in the composition." Applicant respectfully traverses this rejection.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. *See* M.P.E.P. § 2143. First, the prior art reference or combination of references must teach or suggest all the claim limitations. *See In re Wilson*, 165 U.S.P.Q. 494 (C.C.P.A. 1970). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in order to arrive at the claimed invention. *See In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Third, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143.

In the present case, the Action has not established a *prima facie* case of obviousness. Davies proposes a dextrin derivative, in which a proportion of the hydroxyl groups in the dextrin derivative have been replaced by strongly acidic groups, wherein the dextrin derivative is useful in treatment of poisoning or drug overdose. *See* Abstract.

Applicant submits that Davies does not teach or suggest all the claim recitations of the present invention. The present invention relates to a polysaccharide dextrin useful for preventing or reducing the incidence of adhesions in or associated with a body cavity as recited in Claim 1. Alternatively, Davies proposes a dextrin sulphate composition (i.e., **not** dextrin) for use in treating paraquat poisoning by using the composition in a peritoneal dialysis technique wherein the peritoneum is used as the dialysing membrane.

More specifically, Davies proposes that the dialyzing fluid composition is introduced via a catheter into the peritoneal cavity, where it remains for a prescribed length of time, and then is removed by draining out. The Davies invention describes the adsorption of the paraquat onto the **dextrin sulphate** molecule, (Col 2, lines 21-22) reducing the free concentration of the former once in the cavity (Col 2, lines 24-25). In this instance, the cycle is repeated until blood toxins have been removed from the blood and the body, in general.

See Col 6, line 65. Applicant notes that this is not the case with the present invention where typically, dextrin remains in the body cavity until naturally metabolized to maltose and glucose, and no dialysis procedure is performed. Moreover, Applicant notes that it is the **dextrin sulphate** composition of Davies, not dextrin per se, that appears to be effective with respect to the goals of Davies. *See* Col. 1, lines 21-23. Applicants further note that Paraquat is a strong base which typically binds with relatively high affinity to dextrin sulphate but not to dextrin. These observations are further illustrated in Davies at Examples 8, 9, and 10. Moreover, Davies states "[t]hese results demonstrate that paraquat crosses the semi-permeable membrane of the dialysis bag and is **adsorbed by dextrin sulphate but not dextrin** held within the dialysis bag." Col. 5, lines 44-47 (emphasis added). Thus, the present invention is directed toward a distinct dextrin derivative specifically formulated for use for a biologically distinct process.

Applicant further submits that Davies does not provide sufficient motivation to modify its teachings to arrive at the present invention. Where Davies proposes a dextrin derivative formulated for the treatment of poisoning or drug overdose, one of ordinary skill in the art would not be motivated to use the proposed dextrin derivative of Davies as a composition useful for preventing or reducing the incidence of adhesions in or associated with a body cavity as recited in Claim 1. Applicant notes that paraquat is not believed to cause peritoneal adhesions, and therefore, this problem was not acknowledged or addressed in Davies. Thus, there is no teaching in Davies that the dextrin composition may be left to dwell in a body cavity so as to separate tissues that might otherwise adhere together. Moreover, in view of the lack of teaching or suggestion, Applicant submits that Davies does not provide a reasonable expectation of success of arriving at the present invention.

Accordingly, Davies does not teach or suggest all the claim recitations of the present invention, does not provide sufficient motivation to modify its teachings to arrive at the present invention, and does not provide a

reasonable expectation of success of arriving at the present invention. Thus, Davies does not render the present invention obvious under 35 U.S.C. § 103.

B. Claims 1, 3, 11, 14-16, 21, 22, 36, 37, and 39 are patentable under 35 U.S.C. § 103

Claims 1, 3, 11, 14-16, 21, 22, 36, 37, and 39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,587,175 to Viegas et al. (Viegas et al.). More specifically, the Action states at page 4, "it would have been obvious to one of ordinary skill in this art at the time the invention was made having the Viegas patent before him to obtain the claimed composition in view of the closely related structure of the dextrin derivative and similar components present in the composition." Applicant respectfully traverses this rejection.

Viegas et al. proposes an aqueous pharmaceutical vehicle comprising representative film forming polymers that include, but are not limited to polydextrose, cyclodextrin, maltodextrin, dextran, and polydextrose. *See* Col. 6, lines 33-35. However, Viegas does not teach or suggest a composition for preventing or reducing the incidence of adhesions in or associated with a body cavity comprising an aqueous formulation containing the **polysaccharide dextrin in an amount effective to prevent or reduce such adhesions, wherein the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent** to maintain a volume of the aqueous formulation in the body cavity serving to separate tissues which otherwise may adhere to each other as recited in Claim 1. Instead, Viegas et al. proposes a film forming gel which gels *in situ* and may be used as a corneal and ophthalmological treatment. More specifically, Viegas proposes the formation of a **protective layer** between two apposing surfaces or as a cover to a single surface (to achieve drug delivery, for example). Thus, Viegas et al. may provide a physical barrier (or delivery membrane) between untraumatized surfaces.

In contrast, the present invention provides a composition and method to address a sequence of pathophysiological changes taking place between one or two traumatized surfaces. The latter effect is not achieved through barrier means but by a hydroflotation of the general area. In this instance, dextrin may serve as an osmotic agent to establish a continued presence of an aqueous formulation in a body cavity. As disclosed on page 5 lines 23 to 31 of the present application, compositions of the present invention may offer advantages over films and patches of the prior art. Such advantages appear to lie in the observation that adhesions may occur not only at an operative site but also at areas remote therefrom. It is important to note that it is impractical to apply films to an entire area over which damage may occur, whereas with the composition of the present invention, protection of the entire area is achievable. Thus, one of ordinary skill in the art desiring to prevent adhesions in a body cavity, particularly by an osmotic agent that maintains a volume of an aqueous formulation sufficient to separate tissues which might otherwise adhere to each other, would not look to Viegas et al. for guidance. Applicant further noted that Viegas et al. also does not suggest modification of its teachings to arrive at the present invention.

Applicant submits that where Viegas et al. fails to teach or suggest all the claim recitations of the present invention, fails to suggest modification of its teachings to arrive at the present invention, and fails to provide a reasonable expectation of success of arriving at the present invention, Viegas et al. does not render the present invention obvious under 35 U.S.C. § 103.

C. Claims 1, 19, and 20 are patentable under 35 U.S.C. §103

Claims 1, 19, and 20 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,230,933 to Apfeld et al. (Apfeld et al.). More specifically, at page 5 the Action states, "it would have been obvious to one of ordinary skill in this art at the time the invention was made having the Apfeld patent before him to obtain the claimed composition in view of the

closely related structure of the dextrin derivative and similar components present in the composition." Applicant respectfully traverses this rejection.

Apfeld et al. proposes "a novel acid resistant release coated food casing. The invention is particularly useful with acidic casings, particularly tubular nonfibrous casings adapted for processing foodstuffs such as sausages especially frankfurters." Col. 5, lines 33-37. Additionally, Apfeld et al. proposes the following:

> The peeling composition according to the present invention comprises a mixture of a water-soluble cellulose ether such as carboxymethylcellulose with a dextrin. Preferably such composition will also include lecithin and to facilitate formation of self-sustaining, deshirrable, shirred sticks of casing will also preferably contain an anti-pleat lock agent, such as an oil, and a surfactant. Other ingredients may also be utilized e.g. in shirring solutions. Typically employed casing additives are known to the art and may include, for example, humectants, antimycotics, lubricants and antioxidants.

Col. 4, lines 33-48. Thus, Apfeld et al. clearly does not teach or suggest a composition for preventing or reducing the incidence of adhesions in or associated with a body cavity comprising an aqueous formulation containing the polysaccharide dextrin in an amount effective to prevent or reduce such adhesions, wherein the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to maintain a volume of the aqueous formulation in the body cavity serving to separate tissues which otherwise may adhere to each other as recited in Claim 1.

For the reasons stated above in Section III. B., film-forming compositions are typically inappropriate for preventing adhesions. Moreover, Apfeld et al. does not provide sufficient motivation to arrive at the present invention. Applicant respectfully submits that one of ordinary skill in the art would not be motivated to use a composition of Apfeld et al. specifically formulated for food casing as a composition for preventing or reducing the incidence of adhesions in or associated with a body cavity comprising an aqueous formulation containing the polysaccharide dextrin in an amount

effective to prevent or reduce such adhesions as recited in Claim 1, wherein the composition employed comprises an osmotic agent that maintains a volume of an aqueous formulation sufficient to separate tissues . Additionally, in view of the lack of guidance associated with Apfeld et al., Applicant submits that Apfeld et al. does not provide a reasonable expectation of success of arriving at the present invention as recited in Claim 1. Thus, Apfeld et al. does not render the present invention obvious under 35 U.S.C. § 103.

D. Claims 23-35 are patentable under 35 U.S.C. § 103

Claims 23-35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Viegas et al. in view of U.S. Patent No. 4,886,789 to Milner (Milner). More specifically, the Action reiterates the characterization of Viegas et al., and states at page 6, that "it would have been obvious to one skilled in the art at the time the invention was made to prevent adhesion of organs during the healing process as disclosed in the Viegas patent by applying the dextrin to the peritoneal cavity in view of the recognition in the art, as suggested in the Milner patent, that dextrin does not pass from the abdominal cavity through the peritoneal membrane and thus does not cause a rapid drop in the osmotic pressure." Applicant respectfully traverses this rejection.

Contrary to the assertions of the Action, Viegas et al., alone or in combination with Milner, does not teach or suggest the present invention and does not provide a reasonable expectation of success of arriving at the present invention. As stated above, Viegas et al. does not propose a composition comprising an aqueous formulation containing the polysaccharide dextrin in an amount effective to prevent or reduce such adhesions, wherein the dextrin contains more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to maintain a volume of the aqueous formulation in the body cavity serving to separate tissues which otherwise may adhere to each other as recited in Claim 1. Milner is directed to a peritoneal dialysis composition containing an osmotic agent comprising a glucose polymer mixture, wherein the mixture

includes at least 15% by weight of glucose polymers having a DP greater than 12. *See* Abstract. Thus, Milner also does not recite a composition for preventing or reducing the incidence of adhesions in or associated with a body cavity comprising an aqueous formulation containing the polysaccharide dextrin in an amount effective to prevent or reduce such adhesions as recited in Claim 1.

Applicant submits that even if combined, Viegas et al. and Milner do not teach or suggest the present invention directed to a composition comprising, *inter alia*, an aqueous formulation containing the polysaccharide dextrin as recited in Claim 1. Milner concerns a peritoneal dialysis composition comprising a glucose polymer mixture and does not supply the missing recitations necessary to arrive at the composition for preventing or reducing the incidence of adhesions in or associated with a body cavity comprising an aqueous formulation containing the polysaccharide dextrin in an amount effective to prevent or reduce such adhesions as recited in Claim 1. Moreover, Milner proposes a dextrin-based peritoneal dialysis composition that may remain in a body cavity for "as long as eight hours." Col. 11, line 19. In contrast, the composition disclosed by the present invention may remain in the body cavity for a minimum of 2-3 days and up to 7-8 days. *See* Present Application, page 4, lines 24-28. As such, there is a clear difference contemplated in the length of treatment as proposed by Milner and that of the present invention. This difference is reflective of the distinct nature of the compositions of the present invention as compared to the compositions of Milner.

In view of the foregoing, Applicant submits that Viegas et al., alone or in combination with Milner, fails to teach or suggest all the claim recitations of the present invention, suggest modification of its teachings to arrive at the present invention, or provide a reasonable expectation of success of arriving at the present invention. Accordingly, Applicant respectfully submits that Viegas et al., alone or in combination with Milner, does not render the present invention obvious under 35 U.S.C. § 103.

For at least the foregoing reasons, Applicant respectfully submits that the Action fails to establish a *prima facie* case of obviousness under 35 U.S.C. § 103, and requests that this rejection be withdrawn.

IV. Conclusion

In view of the foregoing remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. Any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,

E. Michael Sajovec
Registration No. 31,793

CERTIFICATION OF FACSIMILE TRANSMISSION UNDER 37 CFR 1.8

I hereby certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office via facsimile number (703) 308-4556.

Vickie Diane Prior
Date of Signature: October 3, 2002

Version With Markings To Show Changes Made

In the Specification:

Please replace the paragraph at page 1, line 21 through page 2, line 3 with the following replacement paragraph:

-- WO 92/21354 describes a surgical adhesion as the attachment of organs or tissues to each other through scar tissue. A formation of scar tissue is described as a normal sequel to surgery or other tissue injury and is required for proper wound healing. In some cases, however, the scar tissue overgrows the intended region and creates surgical adhesions. These scar tissue surgical adhesions restrict the normal mobility and function of affected body parts. The invention disclosed in WP 92/21354 is based on the discovery that anionic polymers effectively inhibit invasion of cells associated with detrimental healing processes, i.e. **[ie]**, fibrosis, and **[scaring]** scarring. In particular, certain inhibitory anionic polymers are useful to inhibit fibroblast invasion, thus regulating the healing process and preventing fibrosis. Anionic polymers specified in WO 92/21354 include dextran sulfate, pentosan polysulfate as well as natural proteoglycans, or the glycosaminoglycan moieties of proteoglycans, including dermatan sulfate, chondroitin sulfate, keratan sulfate, heparan sulfate, heparin and alginate. --

In the Claims:

Please amend the following claims:

22. (Amended) A composition according to Claim 1 which further comprises **[includes]** a compound selected from the group consisting of **[one or more of the following compounds,]** glycosolaminoglycan, an antibiotic agent, prostacyclin or an analogue thereof, a fibrinolytic agent or an analogue thereof, an anti-inflammatory agent or an analogue thereof, dextrin sulphate and**[/or]** methylene blue.

23. (Amended) A method of preventing or reducing the incidence of adhesions in or associated with a body cavity, comprising **[which comprises]**

introducing into the body cavity a composition comprising an aqueous formulation further comprising a **[containing the]** polysaccharide dextrin in an amount effective to prevent or reduce the incidence of such adhesions, wherein the dextrin comprises **[contains]** more than 15% of polymers with a degree of polymerization (DP) greater than 12 and acts as an osmotic agent to maintain a volume of the aqueous formulation in the body cavity serving to separate tissues which otherwise may adhere to each other.